Determination of Detection Limits Using Laboratory QC Revision 8: March 25, 2007

DEFINITIONS:

Critical Value (Lc): the statistically estimated measured value of a substance that has less than a 1% probability of being exceeded in a method blank.

False Negative Quality Sample (FNQS): a low level laboratory control QC sample (LCS) used to establish the recovery and reliability of a measurement near the detection limit. The concentration of the FNQS is set at 2-5[1] times Lc but preferably no more than 2 times the regulatory reporting limit, if one exists. The relative standard deviation (RSD) at the FNQS should fall between the limits of 10% and 25%.

FNQS Recovery: percent recovery of the FNQS result calculated as 100*(Measured Value)/(True Value) and includes both random and systematic error. The average FNQS Recovery when N> 20 provides an estimate of measurement bias at the FNQS concentration. Individual FNQS recoveries should fall within the limits of 50%-150%.

RLc[2]: Lc calculated from the variance in FNQS recoveries[3] using the calculation equation[4]:

RLc = t*S(Rec)*Median(FNQS)/Median(Rec)

Where t = Student's t value (n-1 degrees of freedom and alpha = 0.01), S(Rec) = standard deviation of FNQS recovery, Median(FNQS) = median FNQS value, Median(Rec) = median FNQS recovery.

OVERVIEW:

The determination of detection limits is a process of estimating the measurement error in the region of zero concentration[5] for a specified analyte and associated method. This measurement error may be estimated from the standard deviation of the analysis of method blanks[6] when the method blanks generate numerical results. In the absence of method blank results fortified blanks (FNQS) may be used instead. The protocols in this SOP describe the use of FNQS derived detection limits. Since standard deviations may increase with increasing concentration, detection limits estimated from FNQS results will generally exceed those estimated from method blanks. Regardless of whether method blanks or fortified blanks are used, collect data over a period of several days (to include variation in measurement error from day-to-day). Carry all samples though the complete preparatory and analytical process. All data used must meet

The procedure described below uses FNQS data and the associated recoveries generated as batch quality control (QC) results. These QC samples together with the calculated recoveries are used as an assessment of false negatives and provide protection against measurements below the detection limit when the true concentration exceeds the detection limit. The concentrations of the FNQS samples have been adjusted to a concentration range of 2 to five times the estimated detection limit.

PREPARATION and ANALYSIS OF FNQS SAMPLE:

1. Prepare or purchase a stock standard so that a 1:1000 dilution will provide FNQS concentrations not less than twice pre-existing RLc[7] values nor larger than the regulatory limit for regulated analytes. The final FNQS concentration of individual analytes after dilution should be in the range of 2-5 times detection. See Table I for an example. Round values to one significant figure.
2. Dilute the FNQS stock standard solution 1:1000 to prepare the FNQS sample. Prepare this sample fresh daily or per preparatory batch.
3. Prepare and analyze one FNQS sample per analytical batch. If multiple preparatory batches are combined into a single analytical batch, only one preparatory batch is required to contain an FNQS sample.
4. Process the FNQS as a QC sample through all preparatory and analytical steps.
5. Follow the instruction in the method SOP for corrective actions. In the absence of instructions in an SOP, qualify FNQS recoveries outside the limits of 50% to 150% with the qualifier "N."
6. FNQS results must meet all qualitative identification criteria as specified in the analytical SOP.

Table I: Example FNQS Stock Solution Concentration EPA 200.7

	RLc Prior value (ug/L)	FNQS Desired (ug/L)	Stock[8] Undiluted (mg/L)	FNQS Working 1:1000 (ug/L)
Ag	6	20	**30**	**30**
Al	25	80	**100**	**100**
B	10	30	**30**	**30**
Be	1	3	**4**	**4**
Ca	25	80	**80**	**80**
Cd	2	6	**10**	**10**
Cr	7	20	**30**	**30**
Cu	6	20	**30**	**30**
Fe	18	60	**50**	**50**
Mg	33	100	**200**	**200**
Mn	1	3	**4**	**4**
Ni	4	10	**30**	**30**
Pb	8	20	**30**	**30**
Sb	29	90	**100**	**100**
Zn	5	15	**20**	**20**

FNQS EVALUATION AND DETECTION CALCULATION

1. Collect FNQS data by analytical method, matrix category, and date range for the specified method.
2. FNQS data include count of results, median FNQS result, standard deviation of FNQS recovery, and median FNQS recovery.
3. Exclude FNQS recoveries outside the control limits. If control limits do not exist, use 50%-150%
4. Create a spreadsheet using the format in Table III, below, where column A is the count of measurement records, column B is the analytical parameter, column C is the median FNQS, column D is the standard deviation of the FNQS recovery, column E is the median recovery, column F is student's-t[9], column G is the calculated RLc, and column H is percent false negatives (PFN).
5. The formula for RLc in Excel is: =TINV(0.02,count-1)*(Median FNQS)*(Sigma FNQS Rec)/(Median FNQS Rec). The Excel formula for PFN is = 100*TDIST((FNQS-RLc)/(0.01*FNQS*Sigma Recovery/Median Recovery),N-1,1)," ") when LCL < RLc. LCL = FNQS – 3*FNQS*(Sigma Recovery/Median Recovery). Excel formulae are included in a spreadsheet template as a separate document.
6. Report the RLc values together with the associated median recoveries.

EVALUATION OF RLc Results:

1. RLc values calculated from fewer than 20 FNQS results are tentative and must be replaced when more data become available.
2. RLc values should not exceed previously determined RLc values by a factor of more than 1.5 when 20 or more FNQS results are used. RLc values should not exceed RLc values by more than a factor of four (4) for RLc values determined using 7 FNQS results. If RLc values exceed these guideline ranges, the FNQS concentrations can be reduced to achieve lower detection limits depending on the reporting Data Quality Objectives.
3. The ratio of FNQS to the calculated RLc values should be in the range of 2-5. Ratios higher than 5 indicate an FNQS concentration that is too high and should be decreased. Ratios lower than 2 indicate an FNQS concentration that is too low and should be increased. If a regulatory reporting limit has been established, the FNQS should not be set at a concentration exceeding twice the regulatory limit.
4. Recovery rsd values less than 10% indicate an FNQS concentration that can be lowered to achieve a lower RLc and recovery rsd values exceeding 25% indicate an FNQS concentration that is too low and may lead to more than 1% false negatives.
5. Flag RLc values in the calculation spreadsheet if more than 20% of the recovery results exceed the pre-established 50-150% control limits. Flagged RLc values indicate that the selected FNQS concentration cannot achieve the control limits and either the FNQS concentration should be increased or the control limits revised. Note that individual FNQS results below the lower control limit may indicate that associated sample non-detects are false negatives. FNQS results outside control limits must be qualified to indicate the potential for false negatives. When more than 10% of the FNQS recoveries for a multi-analyte method exceed the control limits any batch non-detects should be considered as false negatives. Corrective actions include re-prepping and reanalysis if samples are still available.
6. Calculate the upper control limit (UCL) and lower control limit (LCL) for the FNQS from the equations UCL = median FNQS + 3 standard deviations and LCL = median FNQS – 3 standard deviations[10]. If the LCL or UCL lie outside the DQO established control limits (50%-150%), calculate the percentage false negatives from the equation 100*TDIST((FNQS-RLc)/(0.01*FNQS*Sigma Recovery/Median Recovery),N-1,1). If the percent false negatives exceed 5%, increase the FNQS concentration.

CHECKING FOR MATRIX EFFECTS:

1. If matrix effects are a concern for samples with concentrations below quantification (i.e., concentrations below 3 times RLc), fortify a field sample as a matrix-FNQS sample.
2. Prepare the matrix-FNQS (MS-FNQS) by fortifying a split field sample aliquot in the same manner as for an FNQS QC sample. If precision is also a concern, prepare a second aliquot as an MSD-FNQS.
3. Process the MS-FNQS thru all preparatory and analytical steps.
4. Calculate the recovery (and precision if MSD-FNQS is analyzed).
5. If the recovery is outside the method-analyte specific control limits for the FNQS, qualify the result indicating that there is a presumed matrix effect. If no control limits exist, use 50%-150%.

BACKGROUND CORRECTION

A measurement must be distinguishable from background to be detected. Detection is defined as the identification of a signal that statistically exceeds the random noise when the method bias is zero. When method bias is not zero, efforts to identify and reduce background bias must be made. If method blanks continue to exhibit positive measurement bias, the detection limit (MDL becomes X + t*S(Recovery)*Median(FNQS)/Median(Recovery) where X represents the average of the method blanks associated with the collection, N, of 20 or more FNQS results used to generate the MDL value.

.If the Instrument Detection Limit (IDL) is always less than the MDL, replace the MDL with the IDL. An example is turbidity where the reading for pure water will be approximately 0.03 NTU, higher than the MDL of 0.02 NTU.

Table II: Example FNQS Based RLc Values for EPA 200.7

N	PARM_STORED	MEDIAN FNQS Rec	Sigma FNQS Rec	MEDIAN FNQS	Student's-t	RLc
62	ALUMINUM	92	11	92	2.7	30
89	ARSENIC	119	15	48	2.6	20
68	BARIUM	99	5	20	2.7	2
62	BERYLLIUM	99	7	8	2.7	1
50	BORON	75	13	14	2.7	6
94	CADMIUM	95	7	8	2.6	2
119	CALCIUM	92	17	92	2.6	50
43	CHROMIUM	106	29	7	2.7	5
9	COBALT	102	15	8	3.4	30
155	COPPER	96	17	19	2.6	9
145	IRON	102	9	102	2.6	20
96	LEAD	101	9	40	2.6	10
81	MAGNESIUM	100	16	81	2.6	40
68	MANGANESE	96	6	19	2.7	3
23	MOLYBDENUM	102	14	21	2.8	8
98	NICKEL	102	8	21	2.6	4
116	POTASSIUM	99	22	99	2.6	60
27	SELENIUM	99	16	79	2.8	40
25	SILICA	100	15	180	2.8	80

[1] 1 When FNQS = 2RLc, the percentage of false negatives at the FNQS will be approximately 1%. As the FNQS concentration increases above this ratio, the percentage of false negatives generated decreases.

[2] Derivation of RLc Equation

Definitions:

(1) Lc = t*S(0)
t = Student's-t (α,N-1)
S(0) = standard deviation of distribution centered at zero
N = number of measurements

(2) Recovery (R) = 100*(Measured FNQS Value)/(True FNQS Value)
R = 100*FNQS/True

Derivation:

1.	FNQS = True*R/100	rearrangement definition (2)
2.	AVERAGE(R) = Σ(R)/N	definition of average
3.	Σ(FNQS) = True* Σ(R)/100	from 1
4.	Σ(R) = 100*Σ(FNQS)/True	rearrange 3
5.	AVERAGE(R) = 100*Σ(FNQS)/N*True	2 + 4
6.	AVERAGE(FNQS) = Σ(FNQS)/N	definition of average
7.	AVERAGE(R) = 100*AVERAGE(FNQS)/True	5 + 6
8.	AVERAGE(FNQS)/MEDIAN(FNQS) = AVERAGE(R)/MEDIAN(R)	linear trans
9.	MEDIAN(R) = MEDIAN(FNQS)*AVERAGE(R)/AVERAGE(FNQS)	from 8
10.	MEDIAN(R) = 100*MEDIAN(FNQS)/True	7 + 9
11.	True = 100*MEDIAN(FNQS)/MEDIAN(R)	rearrange 10
12.	S(FNQS) = S(True*R)	from 1
13.	S(FNQS)= True*S(R)/100	True = constant
14.	S(FNQS) = 100*MEDIAN(FNQS)*S(R)/100*MEDIAN(R)	11+13
15.	Lc = t*100*MEDIAN(FNQS)*S(R)/100*MEDIAN(R)	def+14
16.	**RLc = t*MEDIAN(FNQS)*S(R)/MEDIAN(R)**	cancellation

[3] Using variance of recoveries normalizes bimodal distributions that can be created when replacement standards are at different concentrations from the original standard. It also allows for selecting data in statistical control when control limits are established for recovery results and not for the FNQS results.

[4] When N is small (e.g., 7), a more conservative estimate of Lc is provided by using the Chi-Square distribution factor, K, rather than the Student's-t multiplier. Thus RLc = K*s(FNQS Recovery)*(Median FNQS)/(Median FNQS Recovery). Standard deviations follow a Chi-square distribution and not a Student's-t distribution. The two distributions converge for large N, but are significantly different at small N. For N = 7, t = 3.1 and K = 5.5.

[5] A measurement must be distinguishable from background to be detected. Detection is defined as the identification of a signal that statistically exceeds the random noise when the method bias is zero. When method bias is not zero, efforts to identify and reduce background bias must be made. If method blanks continue to exhibit positive measurement bias, the detection limit (Lc becomes X + t*S(Recovery)*Median(FNQS)/Median(Recovery) where X represents the average of the method blanks associated with the collection, N, of FNQS results used to generate the Lc value.

[6] If method blanks are used in lieu of FNQS results, the equation becomes Lc = t*S(0), where S(0) is the standard deviation of the method blanks. If method blank background correction is allowed, Lc = X + t*S(0), where X = average of method blanks.

[7] For an Initial Demonstration of Proficiency where no prior Lc exists, prepare an FNQS by fortifying a method blank at the same concentration used for the lowest calibration standard, a second at one-half that value, and a third at one-fourth. Use the lowest concentration that provides an identifiable measurement.

[8] As provided by the vendor.

[9] Student's-t is evaluated using the Excel command TINV(0.02,Count-1), where count is in column A of the spreadsheet.

[10] Standard deviation is adjusted for recoveries within the initial control limits of 50%-150%, or S= S(Recovery)*Median(FNQS)/Median(Recovery).